Remarks

Introduction

Claims 1-16 were pending, and claims 7 and 10 have been withdrawn from consideration. By way of this response, claims 1 and 16 have been amended. Support for the amendments to the claims can be found in the application as originally filed, and no new matter has been added. Accordingly, claims 1-16 remain pending.

The Examiner has requested a list of co-pending or related applications. The undersigned is currently unaware of any related application.

Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 1-6, 8, 9, and 11-16 have been rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter not described in the specification to enable a person of ordinary skill in the art to make or use the invention.

Applicant respectfully disagrees and traverses the rejection as it relates to the present claims.

Applicant submits that a person of ordinary skill in the art, such as a person with knowledge of formulation organic chemistry, would be able to make and use the invention as presently claimed based on the teachings of the above-identified application. Using conventional chemical synthesis techniques, which are well-known to such persons of ordinary skill in the

art, the therapeutic component and the efficacy enhancing component can be conjugated by either forming a covalent bond between the two components or by employing a linker (e.g., see page 3, line 21, to page 5, line 2). In addition, as discussed at page 14, lines 17-22, the conjugates of the present claims may be synthesized by known techniques, including those described in Powell et al. and Tsuzuki et al., which have been incorporated by reference in the above-identified application.

Further, the specification of the above-identified application discloses how to use the conjugate. For example, at page 5, lines 17-27, the specification discloses that the conjugates may be administered to a patient to treat a condition, such as an eye condition. The administration can be performed by one of many conventional techniques, including topical administration, oral administration, rectal administration, sublingual administration, nasal administration, and/or intravenous administration. The examples set forth in the above-identified application disclose how conjugates are administered topically to eyes, and how effects of such administration may be monitored.

The Examiner cites *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1400 to support the position that undue experimentation would be required by a person of ordinary skill in the art to make and use the claimed conjugates. But, *In re Wands*, holds that "enablement is not precluded by the necessity for some experimentation such as routine screening". Thus, without analyzing the various "Wands" factors - in *Amgen, Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016, 1027 (Fed. Cir., 1991) the Court held "it is not necessary that a court review all the

Wands' factors to find a disclosure enabling. They are illustrative not mandatory."

It is clear from the above-identified application that applicant has taught how to make and how to use the presently claimed conjugates sufficiently to enable one of ordinary skill in the art to practice the present invention. Applicant submits that any experimentation that may be needed to make or use the conjugates would be to optimize the manufacture and use of the conjugates, and that such optimization would be routine to persons of ordinary skill in the art.

In addition, applicant disagrees that the claimed invention is limited to conjugates of a quinoxaline compound and an efficacy enhancing component. Claim 1 recites a conjugate of a therapeutic component and an efficacy enhancing component. Although the elected species included quinoxaline, applicant reserves the right to present additional species upon the allowance of a generic claim.

Moreover, the Examiner has not provided any evidence to support that statement that it is clear the art is highly unpredictable and unreliable,. Applicant submits that methods of making and using the conjugates of the present claims involve conventional chemical synthesis techniques and conventional therapeutic component administration techniques, as discussed above. Therefore, applicant submits that methods of making and using the conjugates are neither unpredictable nor unreliable.

Applicant submits that when the specification is properly considered as a whole, the specification provides adequate and

sufficient information to enable a person of ordinary skill in the art to make and use the conjugates of the present claims. Applicant has provided examples of the use of certain conjugates encompassed by the present claims. However, examples are not required to determine whether a specification is enabling. The specification must be interpreted as a whole.

Applicant further submits that the specification of the above-identified application does provide a disclosure of dosage forms for the conjugates of the present claims. For example, the conjugates may be provided in topical drops, as disclosed in the examples. In addition, the conjugates of the present claims may be provided in solutions or suspensions in aqueous or non-aqueous liquids, or as oil containing emulsions (e.g., see page 18, lines 19-22). Thus, applicant submits that the specification does sufficiently describe dosage forms of the presently claimed conjugates.

"The enablement requirement is met if the description enables any mode of making and using the claimed invention." *Engel Indus., Inc. v. Lockformer Co.*, 946 F.2d 1528, 1533 (Fed.Cir.1991). Applicant submits that the specification of the above-identified application includes such a description of how to make the claimed conjugates using conventional organic synthesis chemistry and of how to use the claimed conjugates using conventional therapeutic component administration techniques. Thus, because the specification describes at least one mode of making and at least one mode of using the claimed conjugates, applicant submits the enablement requirement of 35 U.S.C. § 112, first paragraph has been satisfied.

In view of the above, applicant submits that the present claims, and claims 1-6, 8, 9, and 11-16 in particular, are sufficiently enabled to comply with 35 U.S.C. § 112, first paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Rejections Under 35 U.S.C. § 112, Second Paragraph

Claims 1-6, 8, 9, and 11-16 have been rejected under 35 U.S.C. § 112, second paragraph as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. In particular, the Examiner has indicated that the term "general" has no probative value.

While not conceding with the rejection or the Examiner's remarks, claims 1 and 16 have been amended by deleting the word "general". Accordingly, applicant submits the rejection has been overcome.

Applicant submits that the use of the word "derivatives" in claim 8 does not render the claim indefinite. For example, a derivative of quinoxaline is an agent that is not structurally identical to quinoxaline, but that functions similarly to quinoxaline. Examples of quinoxaline derivatives are identified at page 9, line 34 to page 10, line 20.

In view of the above, applicant submits that the claims satisfy the requirements of 35 U.S.C. § 112, second paragraph, and respectfully requests that the rejection of the present claims based on this statutory provision be withdrawn.

Rejections Under 35 U.S.C. § 103

Claims 1-6, 8, 9, 11-13, 15, and 16 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Desantis Jr. (U.S. 2001/0047012; hereinafter Desantis) and Collins et al. (WO 01/92288; hereinafter Collins).

Applicant respectfully disagrees and traverses the rejection.

Among other things, applicant submits that the Examiner has not met the burden of proof to establish a *prima facie* case of obviousness. The Office Action fails to indicate where in the prior art, a suggestion or motivation is provided to modify or combine the teachings of Desantis or Collins to obtain the claimed conjugates. Absent such an indication, applicant submits that the rejections under 35 U.S.C. § 103 cannot be properly maintained. The motivation or suggestion to support a rejection under 35 U.S.C. § 103 must be clear and particular (*In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999); emphasis added), and "particular findings must be made as to the reason the skilled artisan, with no knowledge of the claimed invention, would have selected these components for combination in the manner claimed" (*In re Kotzab*, 217 F.3d 1365, 1371, 55 USPQ2d 1313, 1317 (Fed. Cir. 2000)).

Applicant respectfully submits that the prior art fails to provide a clear and particular showing that one of ordinary skill in the art would have been motivated to modify or combine

the teachings of Desantis or Collins to obtain the claimed conjugates.

Desantis does not disclose, teach, or suggest the present invention. For example, Desantis does not disclose, teach, or even suggest a conjugate of any type, let alone, a conjugate of a therapeutic component and an efficacy enhancing component, as recited in the present claims. In direct contrast to the present conjugates, Desantis discloses that separate compounds are separately administered to a patient. Further, Desantis discloses that at least one of the compounds is administered orally (see paragraph 0019). In addition, Desantis discloses a method of treating a person comprises administering at least one glutamate antagonist systemically, and at least one IOP-lowering composition topically to an affected eye (see paragraph 0032).

It is clear from the disclosure of Desantis that the glutamate antagonist and IOP-lowering agent are separate from each other and are administered in separate compositions. Because the glutamate antagonist and the IOP-lowering agent are separate and in separate compositions, and are administered by separate routes, the glutamate antagonist and the IOP-lowering agent cannot form a conjugate. Thus, applicant submits that Desantis actually **teaches away** from pharmaceutical conjugates of any kind, including conjugates as recited in the present claims. "As a general rule, references that teach away cannot serve to create a prima facie case of obviousness." (*McGinley v. Franklin Sports, Inc.* CAFC 8/21/01 citing *In re Gurley*, 31 USPQ2d 1131, (Fed. Cir. 1994)). Thus, applicant submits that a person of ordinary skill in the art would not be motivated to modify Desantis or combine Desantis with Collins.

In addition, even if Desantis were to be erroneously combined with Collins, the combination does not disclose, teach, or suggest all of the elements recited in the present claims.

For example, Collins discloses a conjugate of an antibiotic, such as amantadine HCl, and a transcobalamin- or intrinsic factor-binding agent (TC- or IF-binding agent, respectively). The TC- or IF-binding agent is an agent that binds to a vitamin B_{12} transport protein. Thus, Collins discloses that amantadine HCl is one of many potential therapeutic agents, that may be coupled to a TC- or IF-binding agent.

Collins does not disclose, teach, or suggest the present invention. For example, Collins does not disclose, teach, or even suggest a conjugate comprising an efficacy enhancing component having the chemical formula A recited in the present claims. As discussed above, the amantadine HCl disclosed by Collins is a therapeutic component, not an efficacy enhancing component. In addition, Collins does not disclose, teach, or even suggest why a person of ordinary skill in the art might choose amantadine HCl from the lengthy list of potential antibiotics to couple to the TC- or IF-binding agent.

Moreover, the TC- or IF-binding agent disclosed by Collins has a completely different and distinct chemical structure than the efficacy enhancing component recited in the present claims. The chemical structure of the TC- or IF-binding agent is shown at page 39 of Collins. Thus, the TC- or IF-binding agent disclosed by Collins and the efficacy enhancing component

recited in the present claims are both structurally and functionally different and distinct, one from the other.

Therefore, even if Collins were erroneously combined with Desantis, the combination fails to disclose, teach, or even suggest a conjugate which includes an efficacy enhancing component having the chemical formula A, as recited in the present claims.

In view of the above, applicant submits that the present claims, and claims 1-6, 8, 9, 11-13, 15, and 16 in particular, are unobvious from and patentable over Desantis or Collins, taken alone or in any combination, under 35 U.S.C. § 103.

In addition, each of the present dependent claims is separately patentable over the prior art. For example, none of the prior art disclose, teach, or even suggest the present conjugates including the additional feature or features recited in any of the present dependent claims. Therefore, applicant submits that each of the present claims is separately patentable over the prior art.

Conclusion

In conclusion, applicant has shown that the present claims satisfy the requirements of 35 U.S.C. § 112, and are not anticipated by and are unobvious from and patentable over the prior art under 35 U.S.C. §§ 102 and 103. Therefore, applicant submits that the present claims, that is claims 1-16 are allowable. Therefore, applicant respectfully requests the Examiner to pass the above-identified application to issuance at

an early date. Should any matters remain unresolved, the Examiner is requested to call (collect) applicant's attorney at the telephone number given below.

Respectfully submitted,

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